HHS SBIR PAR-15-121

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The official link for this solicitation is: http://grants.nih.gov/grants/guide/pa-files/PAR-15-121.html

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Department of Health and Human Services

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Solicitation:
PAR-15-121

Close Date:
January 05, 2017 (closing in 445 days)
Topic Number:
PAR-15-121

Description:
Background

The **B**rain **R**esearch through **A**dvancing **I**nnovative **N**eurotechnologies (***BRAIN***) initiative is a Presidential project aimed at revolutionizing our understanding of the human brain. By accelerating the development and application of innovative technologies, researchers will be able to produce a new dynamic picture of the brain that, for the first time, shows how individual cells and complex neural circuits interact in both time and space. It is expected that the application of these new tools and technologies will ultimately lead to new ways to treat, cure, and even prevent brain disorders.

NIH is one of several federal agencies involved in the BRAIN Initiative. Planning for the NIH component of the BRAIN initiative is guided by the long-term scientific plan, "BRAIN 2025: A Scientific Vision," which details seven high-priority research areas and calls for a sustained federal commitment of $4.5 billion over 12 years. This report can be found at http://braininitiative.nih.gov/. This FOA and other FOAs issued in Fiscal Year 2015 are based on careful consideration by the NIH of the recommendations of the BRAIN 2025 Report, and input from the NIH BRAIN Multi-Council Working Group (http://braininitiative.nih.gov/MCWG-Roster.pdf), which held its first meeting on August 25th, 2014 (see http://videocast.nih.gov/summary.asp?file=18555&bhcp=1).

In addition to the National BRAIN initiative, the NIH continues to have a substantial annual investment in neuroscience research. The Institutes and Centers contributing to the NIH BRAIN Initiative (http://braininitiative.nih.gov/) support those research efforts through applications received via parent announcements as well as through specific funding opportunity announcements. Potential applicants to this FOA are strongly encouraged to contact program staff if they have any questions about the best funding opportunity announcement for their research.

Research Objectives

Based on the priority areas identified by the BRAIN 2025, two general technology areas were identified to be appropriate for commercial development and are outlined below. While some of the markets for these products may be small, NIH is supportive of developing these technologies towards sustainable commercial manufacture. This will enable novel hypothesis-driven experiments to understand the brain that are currently infeasible, or will reduce barriers to these experiments that currently are costly, difficult, or take too long to perform widely. This FOA seeks to highlight two central themes for exploration: 1) Technologies to understand the dynamic activity of neural circuits and 2) Novel tools to facilitate the detailed analysis of complex circuits and provide insights into cellular interactions that underlie brain function.

Technologies to understand the dynamic activity of neural circuits.

Although invention and proof-of-concept testing of new technologies is a key component of the BRAIN Initiative, to achieve their potential these technologies must also be optimized through feedback from end-users in the context of the intended experimental use, and scalable manufacture platforms/processes developed to enable reliable, broad, sustainable dissemination and incorporation into regular neuroscience practice. This FOA seeks SBIR applications for optimization and validation of emergent technologies and approaches for large scale recording and manipulation of neural activity, to enable transformative understanding of dynamic signaling in the nervous system.

In particular, we seek exceptionally creative approaches to address major challenges associated with recording and manipulating neural activity, at or near cellular resolution, at multiple spatial and/or temporal scales, in any region and throughout the entire depth of the brain. It is expected that the proposed research may be high risk, but if successful could profoundly change the course of neuroscience research. Technologies may engage diverse types of signaling beyond neuronal electrical activity for large-scale analysis, and may utilize any modality such as optical, electrical, magnetic, acoustic or genetic recording/manipulation. Applications that seek to integrate multiple approaches are encouraged. Where appropriate, applicants are encouraged to integrate multiple domains of expertise, including biological, chemical and physical sciences, engineering, computational modeling and statistical analysis.

Examples of priority topics might include, but are not limited to:

- Probes for Large Scale Sensing and/or Manipulation of Neural Activity in Vivo
- Imaging Instrumentation for Recording and/or Manipulating Neural Activity in Vivo
- Development of Electrodes for Large-Scale Recording and/or Circuit Manipulation in Vivo
- Techniques and Approaches for Recording/Manipulating Neural Activity during Behaviors

Novel tools to facilitate the detailed analysis of complex circuits and provide insights into cellular interactions that underlie brain function

In addition to the topics above, this FOA seeks first-in-class and/or cross-cutting non-invasive or minimally invasive techniques that permit repeated measurements from cells over time in a non-destructive manner. The new tools and technologies should confer a high degree of cell-type and/or circuit-level specificity. Tools/technologies relevant for this initiative are expected to be transformative, either through the development of novel tools or through major advances in current approaches that break through technical barriers and will significantly improve current capabilities. In addition, tools developed through this initiative that can be used in a number of species/model

organisms rather than those restricted to a single species are also highly desired as are tools that can be used in any point in the lifespan.

Examples of priority topics might include, but are not limited to:

- Novel methods (non-genetic and genetic) to deliver active agents to specific neurons in particular neural circuits or brain areas with no or minimal cytotoxic effects.
- Significantly improved viral-mediated gene delivery that targets specific cells or cell types in the nervous system.
- Innovative ways to use multiple vectors to deliver “split” gene products to limit and/or control expression in specific cell types.
- Novel, transgenic methods in multiple model species and for use across the lifespan to allow more refined cell-specific and circuit-specific manipulation.
- Chemical or genetic engineering of BBB-crossing carrier agents (such as tagged antibodies) or other tools) to allow inclusion of specific cargoes (e.g., neuronal activity effectors or sensors)
- Novel methods for non-invasive, targeted access to, or manipulation of, distinct cell types in defined circuits with spatio-temporal control
- Novel trans-synaptic tracers that can work in retrograde and anterograde direction, or deliver cargoes to cells in the nervous system.
- Enhanced temporal and spatial resolution techniques for noninvasive molecular imaging of neuronal cells for in situ brain studies.
- Unique combinations of tools for multiplex analysis and/or manipulation of single cells in situ to maximize data content over many parameters (e.g., RNAs, proteins, metabolites, organelles, electrochemical dynamics, signal secretion/reception/transduction, cytoarchitecture or migratory changes).
- Tools that provide significant advances in sensitivity, selectivity or spatiotemporal resolution of molecules/structures/activities within single cells in the brain and between ostensibly similar cells in situ (e.g., high resolution imaging of molecular interactions within single cells).
- Novel automated and scalable assays for high-throughput analysis of single cells in situ in the brain, including scalability of measured parameters in parallel, cell numbers and/or speed of processing.
- Systems-level single cell dataset analysis, including computational approaches, in the context of a functional circuit.
- New tools and approaches that minimize tissue and cell perturbations so that cell viability is maintained, allowing for multiple repeated measures in the same cell over time.
- Methods for tagging neurons to create identified cells.
- Development of in situ sequencing using FISH and other sequencing methodologies.
- Novel methods for visualizing epigenomic marks in neural cells.

This includes the iterative refinement of emergent technologies and approaches that have already demonstrated their transformative potential through initial proof-of-concept testing, with an end-goal of broad dissemination and incorporation into neuroscience labs.

Projects with non-exempt human subjects research, including clinical trials, are not included in this FOA.

The goal of this FOA is to enable a small business that has accomplished the equivalent objectives of a Phase I SBIR or STTR grant through non-SBIR/STTR funds to initiate the Phase II SBIR stage of development, without needing to perform more early stage, Phase-I-SBIR-type research. For this FOA, the small business should have demonstrated the scientific and technical merit and feasibility of the prototype, including proof-of concept studies in an appropriate in vivo animal model.

This FOA will also not accept ‘regular’ Phase II submissions from SBCs that have received a Phase I SBIR or STTR award from NIH or any other agency that participates in the SBIR/STTR programs for projects for which applicants now seek follow-on research and development funding.

For this FOA, it is expected that the technology, prototype, or method will have passed the proof of

principle stage and that the product has demonstrated feasibility and supports a Phase II effort. Data or evidence of the capability (including a statement of any Phase I-like quantitative milestones), completeness of design, and efficacy must be provided in the application, along with the rationale for selection of the criteria used to validate the technology, prototype, or method, similar to a Phase I final report required in standard Phase II applications.